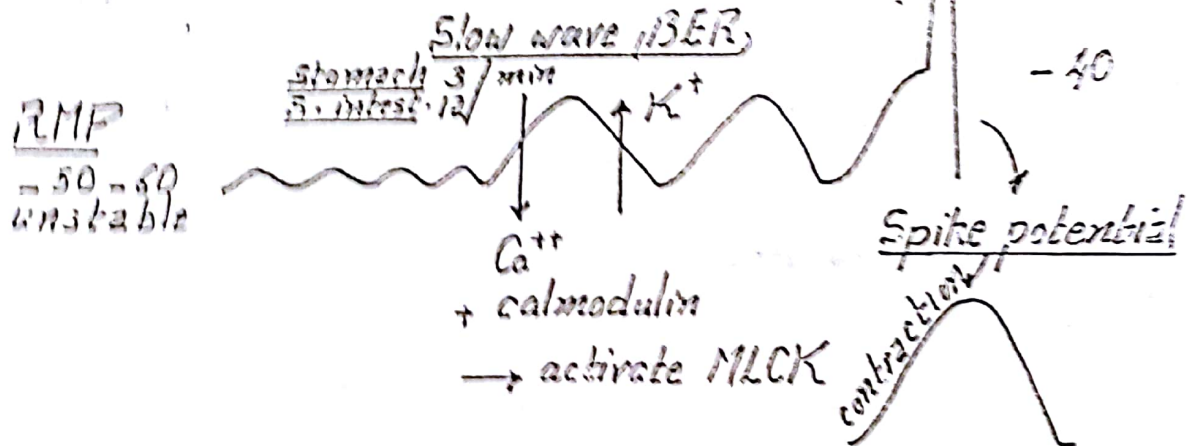


Gastro-intestinal tract

Electrical activity of smooth vs



Depol : stretch, parasympathetic

Hyperpol : sympathetic

Innervation of GIT

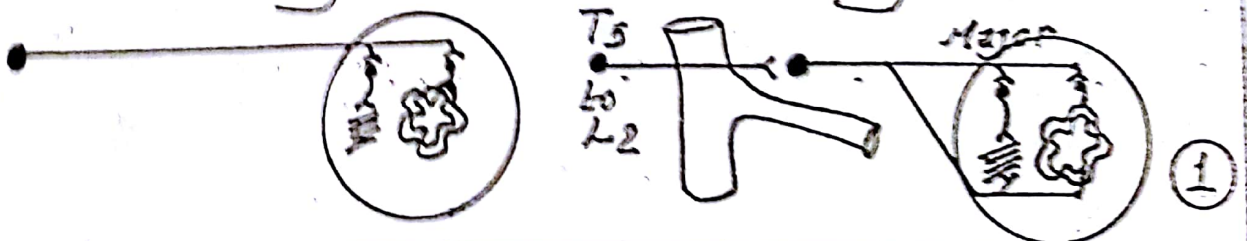
A) Enteric nervous system

1. Motor neurones
 - a Myenteric (Auerbach's) plexus
 - b Submucosal (Meissner's) plexus
2. Sensory neurones
Respond to stretch, tonicity, glucose, aa & interneurones.

B) Extrinsic innervation

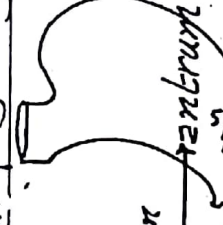
1. Parasymp
Preganglionic
end on plexuses
Excitatory

2. Sympathetic
Postganglionic
end on plexuses (major)
direct on ms & glands
Inhibitory



VISIT...

LANZAROTE
Caliente.COM

	Stimuli	Site	Physiological action	Chem	
1 <u>Gastrin</u>	1 Distension of antrum 2 Soup extract: leptones phenylalanine tryptophan 3 Rise of pH above 2 4 Vagal stim. viz GRP inhibited by - Luminal: ++ acids SS - Blood: GIP & secretin		 1 ++ HCl & pepsin 2 Trophic to GI mucosa 3 Cont. of LES 4 Stim. of G. motility 5 ++ insulin	Chem	<u>Other hormones</u> - Site ----- - Structure ----- <u>VIP</u> vasoactive intes. peptide 1 VD of intest bl. vs 2 ++ intest secretion of electrolytes & H₂O 3 -- HCl secretion 4 ++ panc. NaHCO₃ 5 Relaxation of GI smoothms <u>Motilin</u> 1 Cont. of LES 2 Stim. of enterl and duodenal motility <u>Somatostatin</u> 1 -- Gastrin, GIP, secretin, VIP and motilin 2 -- Gastric secretion. <u>N.B</u> Gastrin family: Gastrin & CCK Secretin, : Secretin, GIP VIP, glicentin & glucagon
2 <u>GIP</u> Gastric inhibitory peptide	-- pH in intest. fluid CHO & Fat		 -- HCl ++ INSULIN		
3 <u>Secretin</u>	-- pH in intest. fluid below 4.5		 -- HCl ++ INSULIN Aqueous large vol rich in NaHCO₃ poor in enzyme i.e augment CCK		
4 <u>CCK</u> cholecyst kinin. Pancreo zymin	aa small peptides Fatty acid Bile salts		 Evacuated G. bladder Enzymatic small vol poor in NaHCO₃ rich in enzymes <u>Other actions</u> 1. Augments secretin 2 Trophic to pancreas 3 -- gastric emptying 4 ++ intestinal motility 5 ++ insulin	Polypeptide (nongonemic) rapid min.	

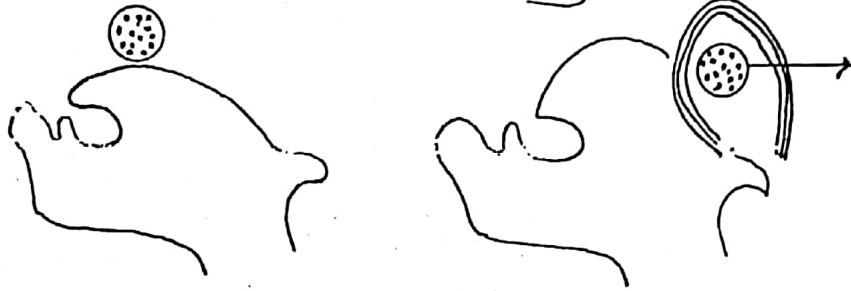
Hormone Items	Gastrin	GIP	Secretin	CCK
Site of release	Upper part of s. intestine (Duodenum & upper part of jejunum).			
	Gastric antrum			
Stimuli	1 Distension of antrum 2 Soup extracts & peptones. 3 Rise of pH above 2 4 Vagal stimulation	1 $\ominus$ pH in intest. Fluid. 2 CHO & Fat.	$\ominus$ pH in intest. Fluid below 4.5.	1 aa, polypeptide & fat. 2 Bile salt.
Physiological actions	1 $\oplus\oplus$ HCl secretion 2 Trophic to GI mucosa 3 Cont. of LES 4 Stim. of G. motility	1 $\ominus$ HCl secretion 2 $\oplus\oplus$ insulin "	1 $\ominus$ HCl secretion 2 $\oplus\oplus$ Panc. aqueous Juice. Large volume rich in NaHCO_3 poor in enzymes	1 Evacuation of G. bladder 2 $\oplus\oplus$ Panc. enzymatic Juice. Small volume Poor in NaHCO_3 Rich in enzymes
VIP		Motilin	Somatostatin	Others actions of CCK
Site of release: Upper part of s. intest.				1 Augments secretin action 2 Trophic effect on pancreas
Actions	1 VD of intes. bl. vs 2 Regulate GI motility 3 $\ominus$ HCl secretion 4 $\oplus\oplus$ Panc. NaHCO_3 5 Relax of GI relax.	1 Cont. of LES 2 Stim of antral & duodenal motility	1 $\ominus$ secretin secretion 2 $\ominus$ gastrin secretion	3 $\ominus$ gastric emptying 4 $\oplus\oplus$ intestinal motility
All G.I hormones increase <u>insulin</u> secretion especially <u>GIP</u>				GIP = Gastric inhibiting peptide CCK = CholecystoAmin VIP = Vaso active intestinal peptide. 3

W

Swallowing Deglutition 3 stages

Centre Medulla

A Buccal Voluntary



B Pharyngeal Involuntary 1-2 second

One out of 4 ways :

- Nose Elevation of soft palate
- Mouth Elevation of tongue
cont of mylohyoid ms
- Larynx Elevation of larynx
closure of glottis
apnea

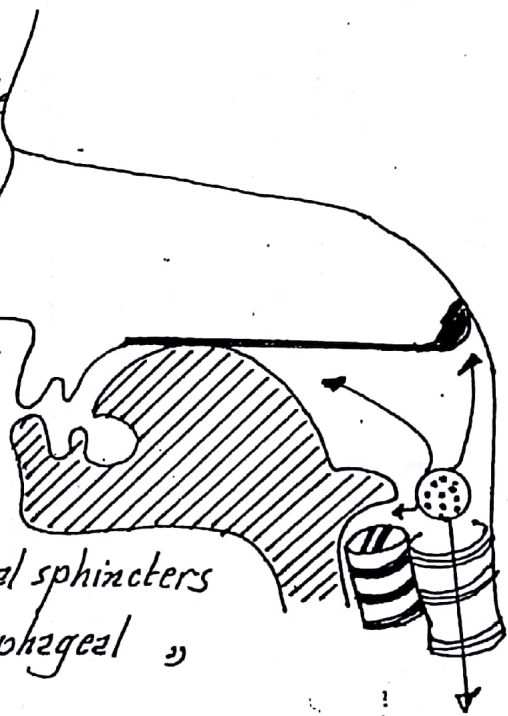
○ Pharynx

Successive cont of pharyngeal sphincters

Relaxation of pharyngo-esophageal "

A reflex act

- Stimulus : food in back of mouth
- Receptors : around openings of pharynx (tonsillar pillars)
- Centre : medulla & lower pons



C Esophageal Involuntary

(4)

Esophageal stage

2 types of peristalsis

- 1 Prim. peristalsis continuation of peristalsis wave in pharynx
8 - 10 second
- 2 Second peristalsis via esophageal distention of retained food.
initiated partly by enteric nervous system
partly by vago-vagal reflex

Function of lower esophageal sphincter Gastro-esophageal sphincter

It remains tonically contracted until receptive relaxation relaxes LES ahead of peristaltic wave which push swallowed food into stomach

The tone of LES is under neural control:

- 1 Acetylcholine from vagus causes contractions of LES.
- 2 NO & VIP from interneurons innervated by vagus causes relax. of LES.

Between meals, normal tonic activity of LES prevents reflux of stomach content into esophagus

Abnormalities of tone of LES

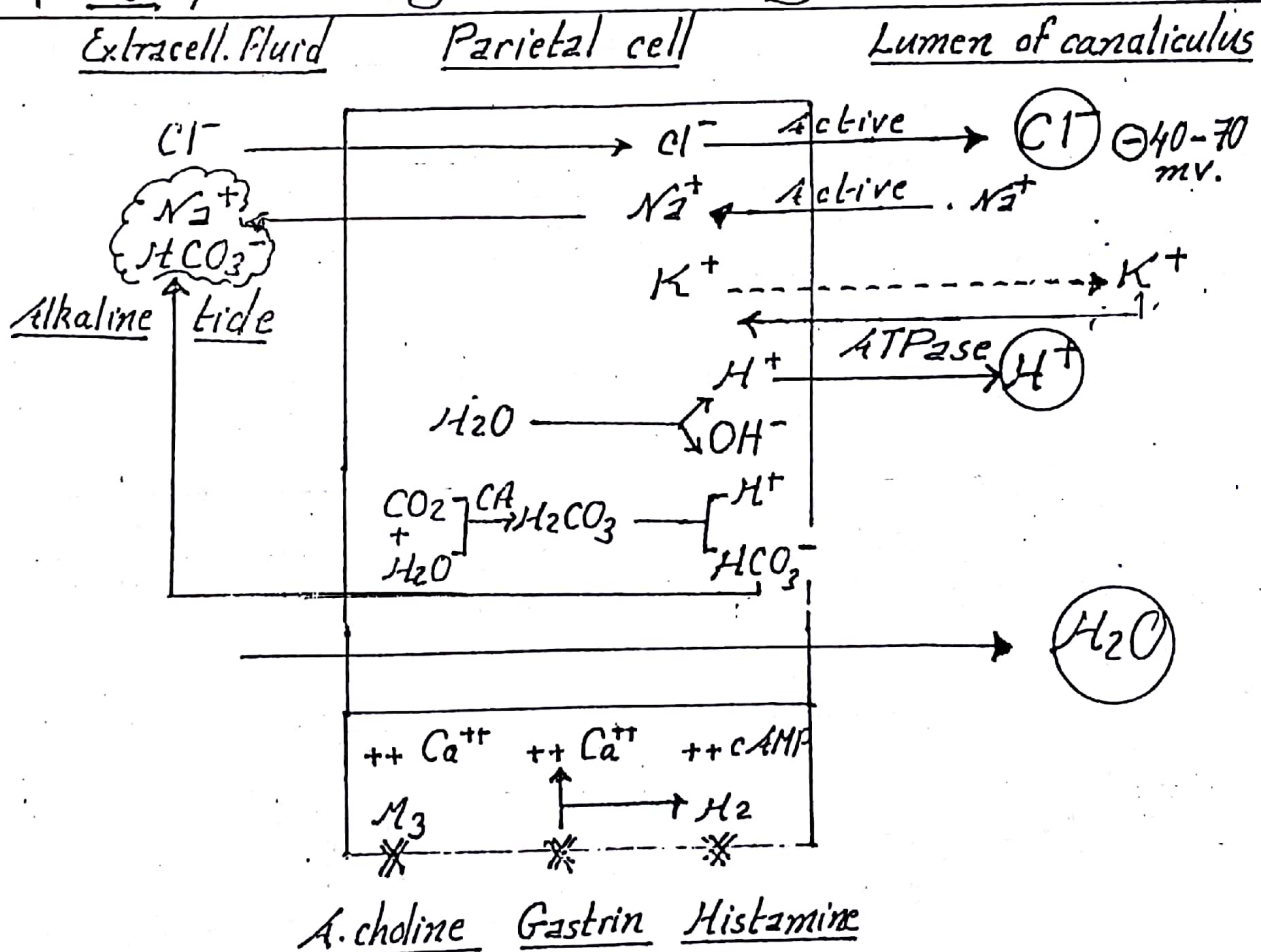
- 1 Decreased tone of LES during pregnancy due to high level of progesterone leading to reflux of gastric acid into esophagus (gastro esophageal reflux) → heartburn, oesophagitis, ulceration & stricture of esophagus by scarring
- 2 Achalasia: Incomplete relaxation of LES → accumulation of food in esophagus → massive dilatation

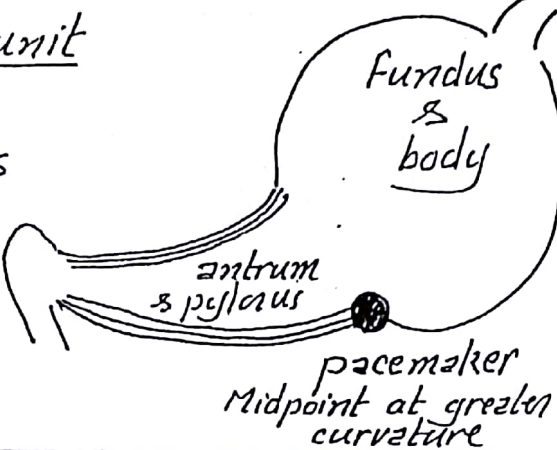
Cause Failure of release of NO and VIP

ttt Dilatation of sphincter, esophageal muscle incision or injection of botulinum toxin in LES to inhibit A.choline release.

Mechanism of acid secretion

- 1 -ve potential -40 to -70 millivolts inside lumen is created by active transport of a Cl^- from cell to lumen & Na^+ from lumen to cell. This leads to passive diff. of K^+ to lumen of canaliculus
- 2 H_2O dissociates into H^+ and OH^- in cell cytoplasm. H^+ is actively secreted to lumen in exchange for K^+ reabsorbed by cell via H^+/K^+ ATPase pump (proton pump)
- 3 CO_2 (from cell & blood) + $\text{H}_2\text{O} \xrightleftharpoons{\text{CA}} \text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+$
 H^+ combines with OH^- released in step 2 to form H_2O
 HCO_3^- diffuses out of cell in exchange for Cl^- then step 1 is repeated
- 4 H_2O passes through cell to lumen by osmosis



<u>Distal motor unit</u> thick wall Mixes & empties BER	 Fundus & body antrum & pylorus pacemaker Midpoint at greater curvature	<u>Proximal motor unit</u> thin wall Stores Receptive relaxation Stimulus G: distension Movement of pharynx & esophagus during swallowing ○ Vago-vagal R
<u>Mechanism of inhibition</u> <u>Depression</u> <u>Fear</u>	<u>Drop of pH below 2</u> ○ <u>Somatostatin</u> paracrine.	<u>Nervous</u> <u>Hormones</u>
<u>Mechanism of G. secretion</u> A) <u>Cephalic</u> 1/3 <u>Nervous</u> [<u>Conditioned</u> / <u>Unconditioned</u>] قبل أثناء بعد	B) <u>Gastric</u> 2/3 <u>Nervous</u> [<u>Long</u> Vago-vagal R / <u>Short</u> Submucosal plexus] <u>Hormonal</u> <u>Gastrin</u>	C) <u>Intestinal</u> inhibitory <u>Nervous</u> <u>Enterogastric R</u> ○ Stimulus ++ acid Duodenal distension <u>Hormones</u> <u>GIP</u>, <u>secretin</u>, <u>CKA</u>, <u>VIP</u> ○ Stimulus <u>fat</u> <u>hypertonic sugar</u> (7)

Pancreatic secretion

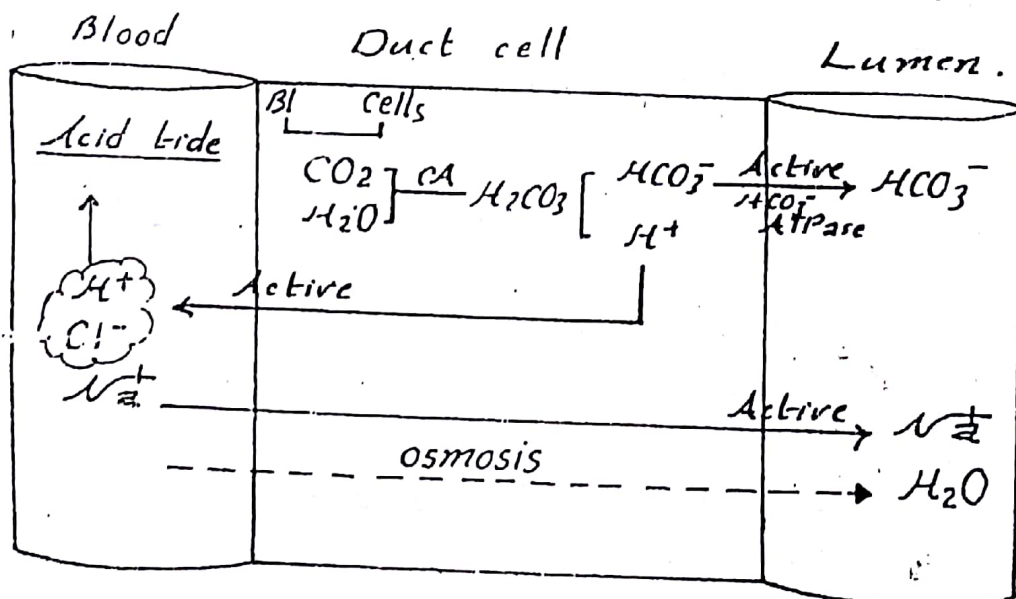
Two types:

<u>Item</u>	<u>Aquous</u>	<u>Enzymatic</u>
<u>Characters</u>	Large volume Rich in NaHCO_3 Poor in enzymes	Small volume Poor in NaHCO_3 Rich in enzymes
<u>Site</u>	Duct cells	Acinar cells
<u>Control</u> - <u>Hormonal</u> - <u>Nervous</u>	<u>Secretin</u> (discuss) ↑ ++ cAMP	CCl ₄ (discuss) ↑ Vagus (ACholine) Phospholipase C

Aquous secretion

- washes out the enzymes.
- provides neutral pH for enzymes.

Mechanism of NaHCO_3 secretion 113 mEq/L



Pancreatic venous blood is acidic.

Pancreatic enzymes

Fully sufficient for complete digestion

o Zymogen granules are formed by cells & discharged by exocytosis

① Starch $\xrightarrow[\text{Active Form}]{\text{Panc. Amylase}}$ maltose

② Neutral fat $\xrightarrow[\text{Active Form}]{\text{a Panc. Lipase}}$ FFA & monoglyceride

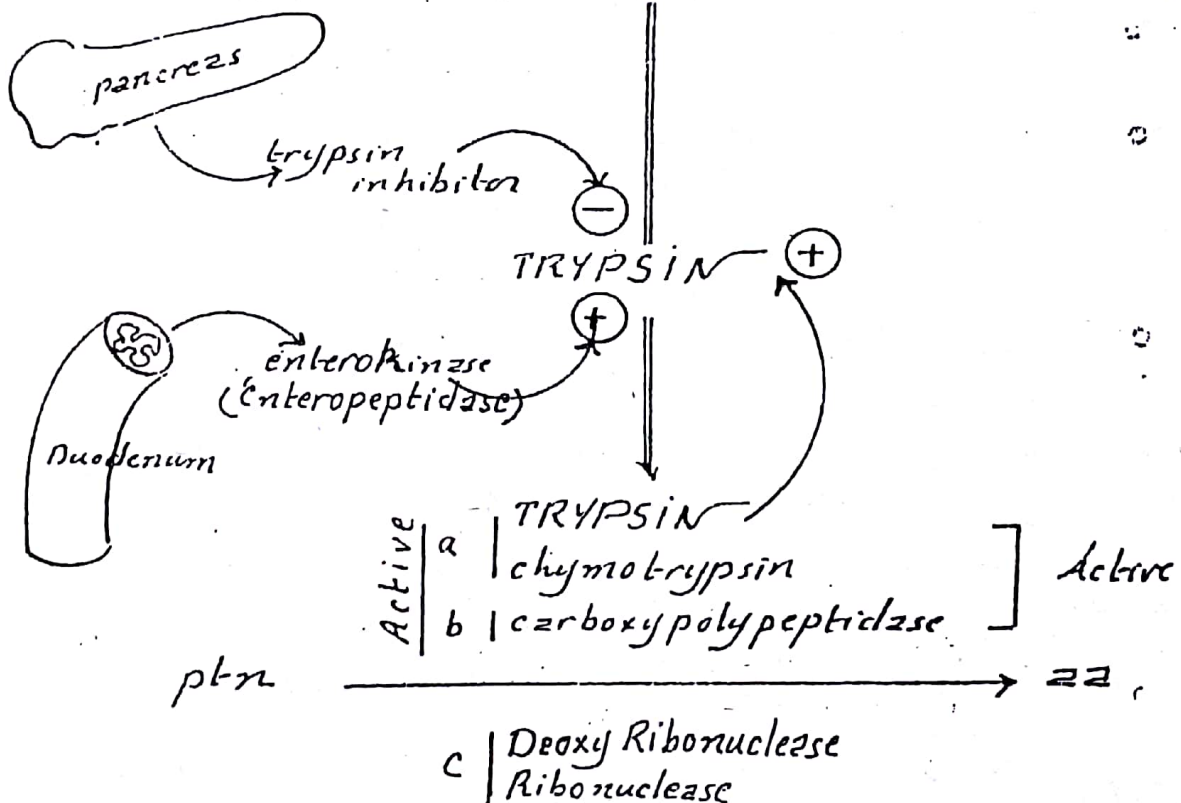
activated by bile salts

b cholesterol esterase

c Phospholipase A $\longrightarrow$ FFA & lysophospholipid

③ Proteolytic enzymes

Inactive	Procarboxypolypeptidase	exopeptidase
	Chymotrypsinogen	endopeptidase
	TRYPSINOGEN	



acute pancreatitis: lethal or life time panc. insufficiency

o Congenital -- enteropeptidase $\longrightarrow$ panc. malnutrition. ⑨ GIT

Liver and biliary system

Functions of the liver

- ① Vascular Function storage 200-400 ml & filtration of blood Kupffer cell
- ② Metabolic Function
 - a CHO Glucostatic mechanism
 - b Fat Lipoproteins, cholesterol & phospholipids
 - c Ptn urea, plasma ptns, nonessential aa
 - d Storage of vitamins A, D & B₁₂
 - e Storage of iron Apoferritin + iron → ferritin
 - f Detoxification & excretion in bile: drugs, hormones & Ca⁺⁺
- ③ Secretory and excretory functions: Formation of bile

BILE

Mechanism of bile secretion

- Between meals: Bile flows into gall bladder

- When food is taken:

- Swallowing relaxes sph. of Oddi

- Food in intestine CCK

- After meals:

- Enterohepatic circ for bile salts

90-95% of bile salts are reabsorbed from terminal ileum

- Mostly by secondary active reab with Na⁺ powered by Na⁺-K⁺ countertransp. at

- Some by non ionic diff

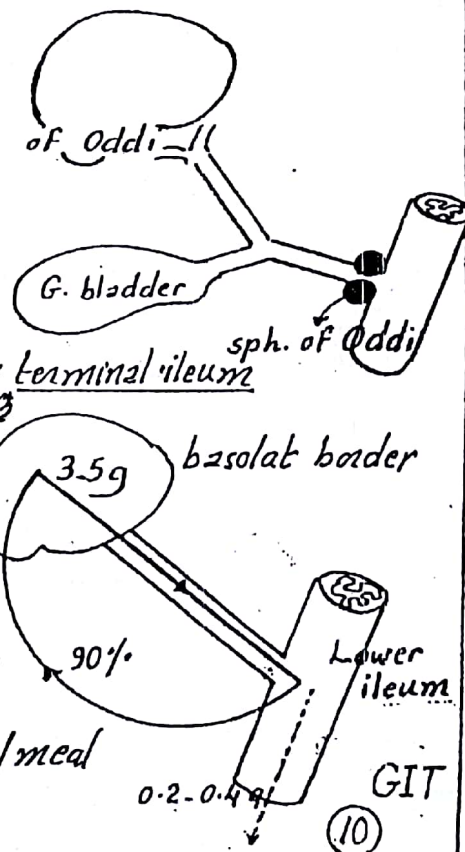
5-10% enter colon & converted to bile salts

- deoxycholic acid: All reabsorbed

- lithocholic acid: 1% "

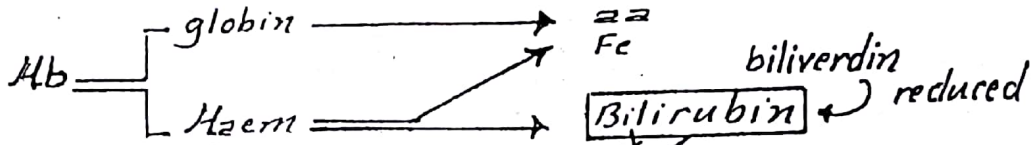
& replaced by liver rest pass to stool
0.2-0.4 g/day

Total bile salts 3.5 g/day recycled by enterohepatic circulation 2 times/meal i.e 6-8 times daily



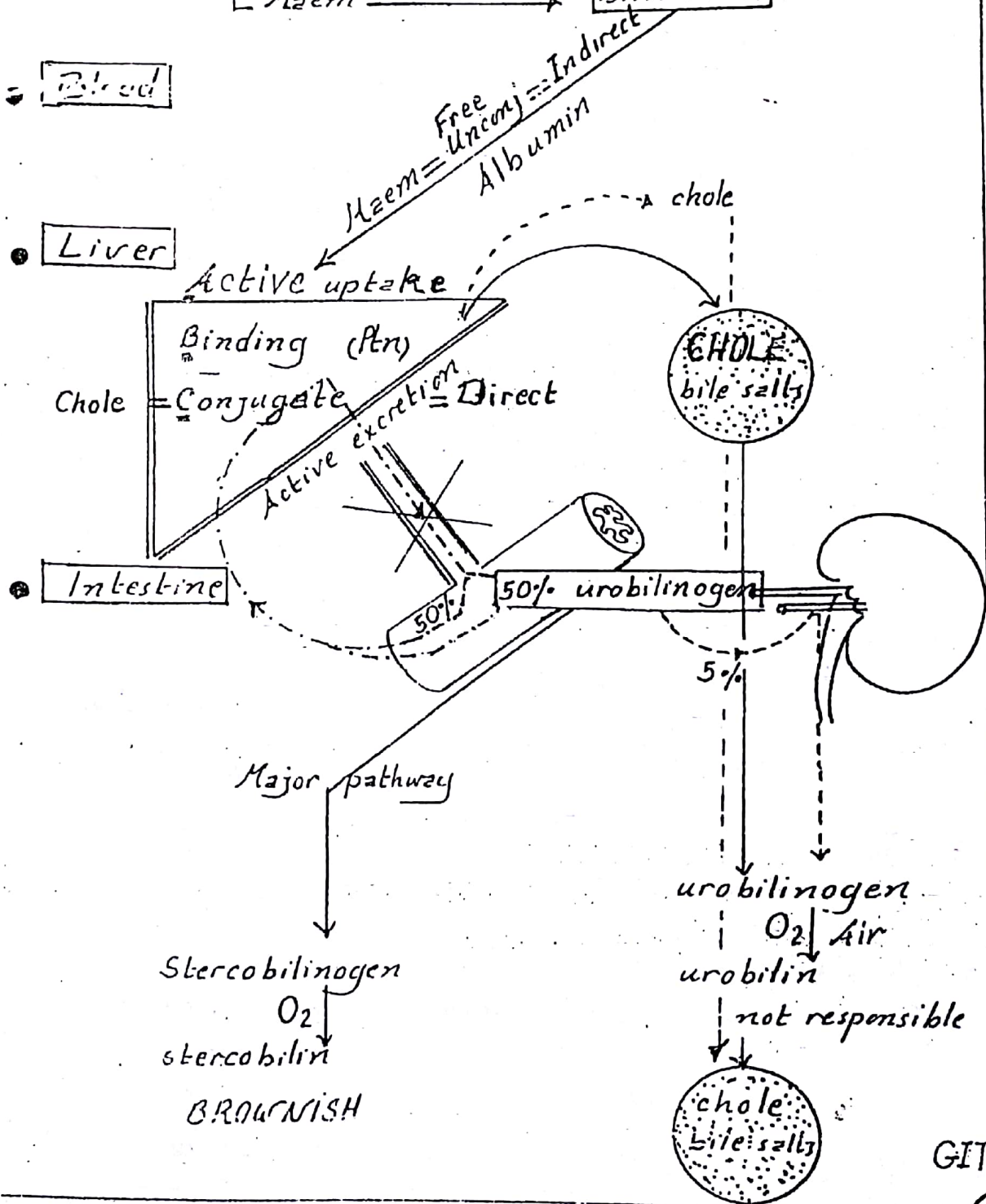
Formation of bile pigment

RES



Blind

Liver

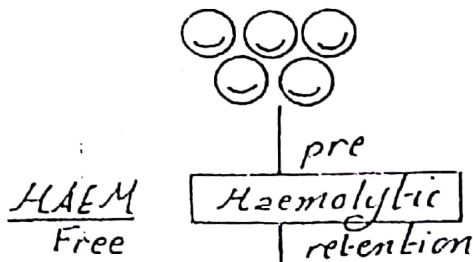


Jaundice

Yellowish tint

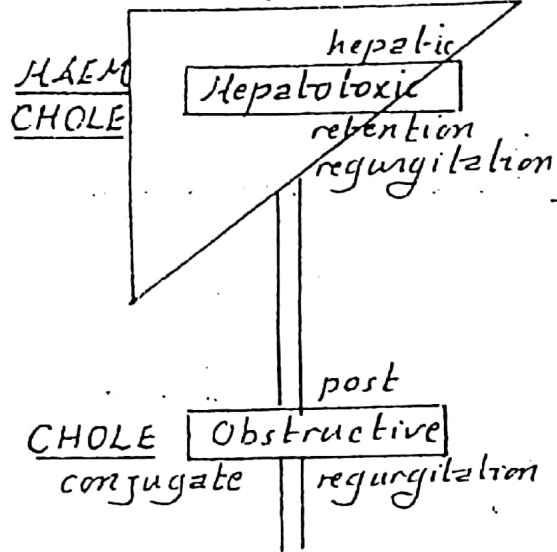
Hyper bilirubin aemia above 2mg%
normally less than 1mg% 0.5mg

Normal



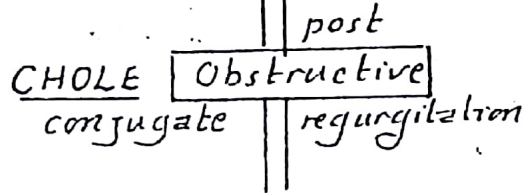
++++ rate of formation of HAEM
++ rate of uptake by liver
++ rate of excretion
↑ stercobilin stool very dark
urobilin urine normal

Impaired



Liver is unable to
- uptake all haem bilirubin
→ retention of HAEM
- excrete chole bilirubin
→ regurgitation of CHOLE
+ bile salts

Cholesterol
Alkaline phosphatase



regurgitation to blood of
CHOLE + bile salts
excretion in urine of
CHOLE + bile salts

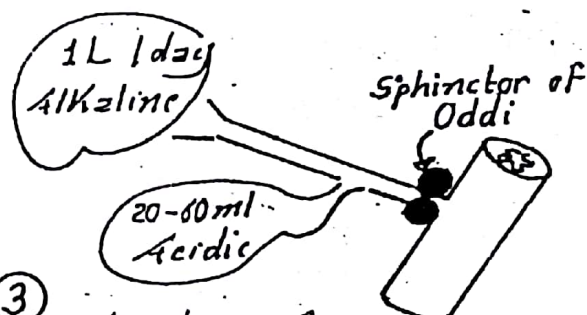
Liver Function Tests

- Hyperbilirubinemia :
HAEM does n't pass in urine no bile salts indirect
CHOLE pass in urine bile salts direct
- Bile salts in blood → pruritis & bradycardia

GIT

Functions of gall bladder

① Storage of bile :



② Concentration of bile & equalization of pressure :

Mechanism : Na^+ ions are actively transported
 Cl^- & HCO_3^- ions follow passively
 H_2O follows passively

Aim : To prevent the increase in biliary P

④ Acidification of bile :

Mechanism : NaHCO_3 reabsorption

Aim : to prevent the ppt of
 lecithin, bile salts & cholesterol.

⑤ Secretion of white bile :

i.e. Mucous

Aim : to prevent the irritation of the mucosa
 by the concentrated acidified bile.

⑥ Evacuation of gall bladder

Hormonal CCK more powerful.

Nervous Vagus stimulation

- Directly cephalic stage

- Indirectly gastric stage

vago-vagal reflex

Small intestine

Secretion of the small intestine

① Intestinal mucus :

Functions :

- covers, protects & lubricates
- binds some bacteria
- holds Igs

Secreted by :

- Surface epith. cells
- Goblet cells
- Brunner's glands

② Intestinal alkaline fluid :

Formed by the epith cells in the crypts of Lieberkühn
Isotonic fluid of NaCl and HCO_3^-

Volume 1800 ml

pH 7.5-8

③ Enzymes :

Not secreted. Present at the brush border.

Peptidases, disaccharidases, intestinal lipase.

Regulation of the small intestinal secretion :

- 1 Nervous : local nervous reflexes most important
- 2 Hormonal : Secretin, CCK, VIP (VIP ++ electrolytes & H_2O)

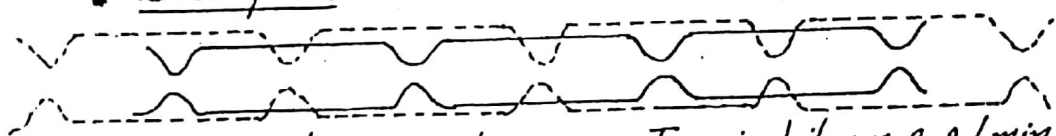
Movements of the small intestine

2 types

① Segmentation (mixing) contractions

most frequent

• Description :



Duodenum 12/min

Terminal ileum 8-9/min.

- Control : Myogenic BER
need the enteric nervous system.

- Functions : 1 Digestion : Mix chyme and juices
2 Absorption : Contact between chyme & mucosa.

③ Migrating Motor Complex (MMC)

Description

Repeated waves of slow peristalsis during fasting

Functions

Moves undigested substance from small intestine
Prevent bacterial growth & multiplication

(14)

② Peristaltic waves :

- Contraction Stretch relaxation
 Substance P CGRP VIP
 A. choline



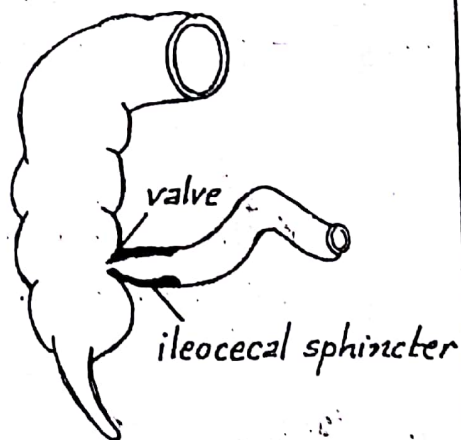
- It depends on the enteric nervous system
- Function Propagation of food

Notes :

- Peristaltic rush very powerful & rapid
 caused by irritation of intestinal mucosa.
 initiated by Extrinsic n reflexes : brain stem.
 Myenteric plexus reflexes
- Peristalsis is blocked if a segment of intestine is reversed
- Intestinal motility ++ gastrin, CCK, serotonin & insulin
 -- secretin & glucagon
- Gastro ————— enteric reflex
 Gastric distension → ++ intestinal peristalsis mediated by myenteric plexus

The ileocecal valve and sphincter

- Relaxation of the sphincter
 - Gastro ileal reflex
 i.e Gastric distension
 - Gastrin hormone
- Contraction of the sphincter
 - Distension of the cecum
 - Irritation of the cecum
 mediated by sympathetic



Large intestine Colon

Innervation of the colon 100 cm

1. Sympathetic : L. splanchnic nerve
 2. Parasympathetic : Proximal half vagus
Distal half pelvic nerve.
- N.B. External anal sphincter : pudendal nerve (somatic n.)

Motility of the colon

Coordinated by slow waves (BER)

1. Mixing movements Ileocecal valve 2/min. Sigmoid 6/min.
- a. Segmentation movements

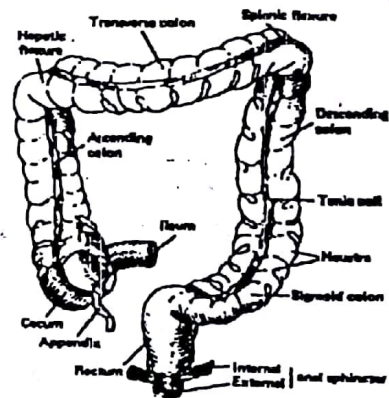
Illustrations

1 & 2 allow the absorption of 90% of the fluid. (1-2 Litre)

- Propulsive movements

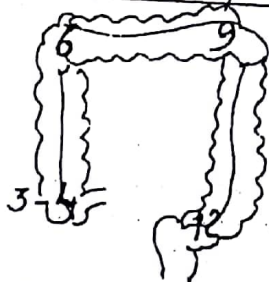
- a. Peristaltic waves : rare
- b. Mass movement : few times/day
contraction of large area.
moves the fecal material en mass.

Controlled by extrinsic autonomic nerves & gastrin



Transit time in the colon

The 1st part of the test meal reaches



the cecum	in 4 hours
the hepatic flexure	in 6 "
the splenic flexure	in 9 "
the pelvic colon	in 12 "
the anus	much slower

Dietary Fibres

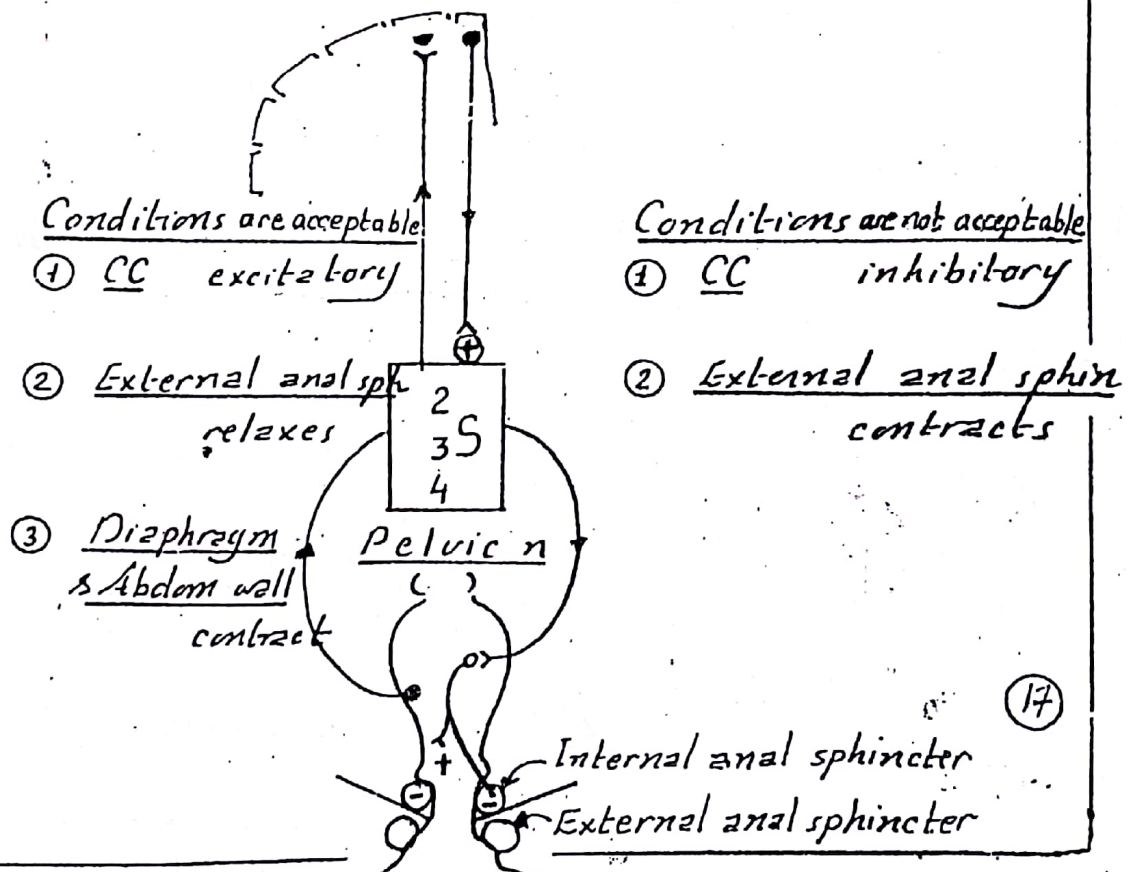
Not digested or absorbed e.g cellulose
Function Bulk laxative work

Colonic bacteria

synthesize vitamin K & a number of B comple.
& produce some of the gases in the flatus

Defecation

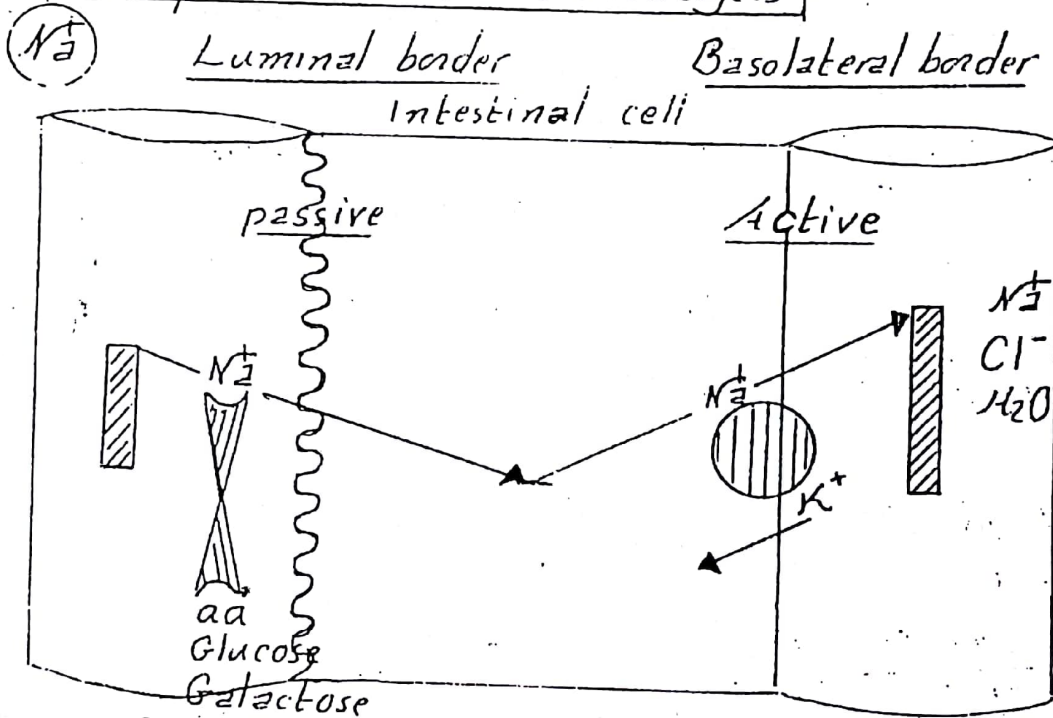
- Preparatory reflex Gastro colic & Duodenocolic R.
Mass movement
- Spinal parasymp. reflex | new born babies
TS of spinal above sacral region
 - Stimulus Distension.
 - Receptors Mechanoreceptors.
 - Afferents Pelvic nerve.
 - Centre 2-3-4 sacral
 - Efferent Pelvic nerve.
 - Response Contraction of wall.
Relaxation of internal anal sphincter.
- Voluntary control of defecation:-



Absorption

- 200 m²
- increased 600 times

Absorption of H₂O & electrolytes



Cotransport

Aldosterone

(K⁺)

- Absorbed by passive diffusion in colon
- Actively secreted (aldosterone) in colon

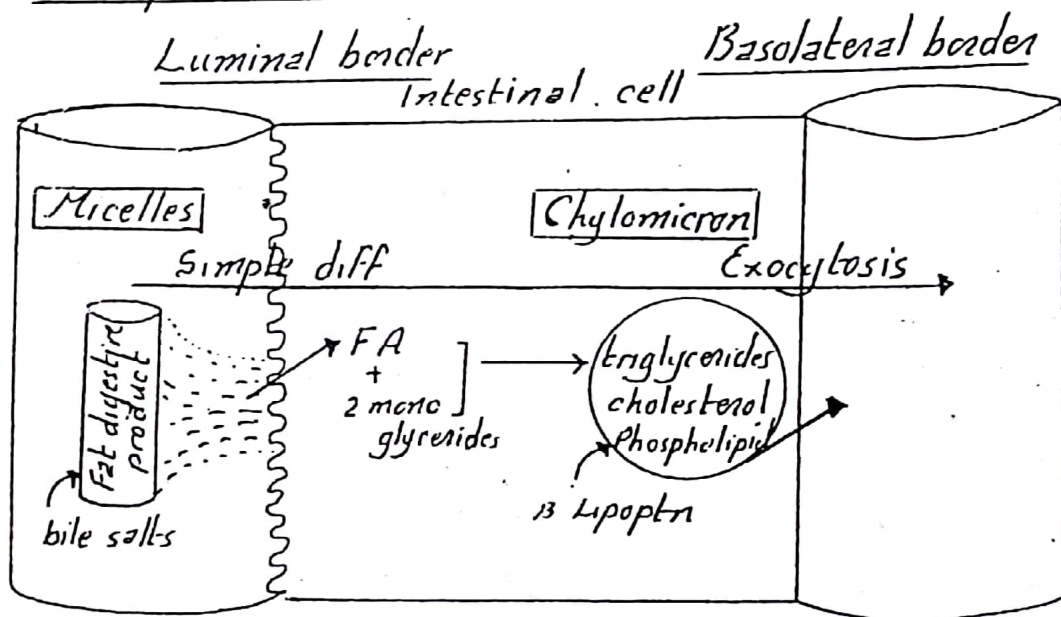
(Ca⁺⁺)

- Absorption in duodenum
- Luminal border: Facilitated diff
- basolateral border: Active transport

(Fe⁺⁺)

- Absorption in duodenum
- Lumen:
 - Vit. C
 - HCl dissolves
- Enterocytes: Apoferritin (pfr) + iron → Ferritin
- Blood: Iron is carried on transferrin

Absorption of Fat



Transport

- Chylomicrons 80-90% in lymphatic
- Short chain FA (more H_2O solub.) in blood.

Absorption of CHO

Luminal border

Cotransport with Na^+

Secondary active transport

Basolateral border

Facilitated diffusion.

Absorption of Ptn

Luminal border

Cotransport with Na^+

Secondary active transport

Basolateral border

Simple or Facilitated diff.

Absorption of vitamins

- Fat soluble vitamins as part of micelles
- H_2O soluble vitamins
 - B_{12} needs intrinsic factor pinocytosis in ileum
 - rest of B vitamins & vit. C Facilitated diff. or Na^+ dependent active transport.

Small intestine

Brush (luminal) border is lined by amorphous layer (glycocalyx) rich in neutral & aminosugars and serve a protective function.

Movements of small intestine

2 Segmentation Mixing contraction

Maximal frequency in duodenum & proximal jejunum 12/min
in terminal ileum 8-9/min

3 Migrating Motor Complex (MMC)

Description: It occurs during fasting & stops by food ingestion. Repeated waves of peristalsis that travel short distance then die out. Each new wave starts slightly lower than the previous one.

The waves slowly migrate down small intestine taking 2H to reach large intestine.

Functions: Moves any undigested substance remaining in intestine.

2 Prevents bacteria from remaining in intestine long enough to grow.

Adynamic (paralytic) ileus

(page 25)

Gall stones (cholelithiasis)

1 Cholesterol stones 85%

Radioltranslucent

Cause altered lecithin, cholesterol (H_2O soluble) to bile salts ratio

2 Ca bilirubinate stones

Radioopaque

Cause Conjugate bilirubin
bact. Free bilirubin + Ca^{++}
→ Ca^{++} bilirubinate
(insoluble)

Causes of jaundice:

- 1 Hemolytic J: Hemolysis i.e hemolytic anemia, drugs, malaria, transfusion reaction & autoimmune dis.
- 2 Obstructive J: Obstruction of bile ducts
 - a Intrahepatic: Liver cirrhosis or acute viral hepatitis
 - b Extrahepatic: Stones, carcinoma or stricture

Digestive system

G.I. smooth muscles are arranged in bundles of 1000 m.f connected by gap junction i.e each muscle layer functions as syncitium.
Excitation wave travels few mm up to entire length of intestine.
Connection exists between the longitudinal & the circular m. layers
Electrical activity of G.I. smooth ms : SLOW 2 types :

- RMP unstable 50-60 mvol.
- Depol. occurs by parasymp. stim or stretching of muscle.
- Hyperpolarization occurs by sympathetic stimulation.

① Slow waves : basic electrical rhythm BER.

Description : Slow change in RMP (not A. potentials).

Mechanism : Gradual depol. (Ca^{++} influx) then gradual repol. (K^{+} efflux).

Rate : 3/min in stomach & 12/min in small intestine

Initiated by : Pacemaker cells (interstitial cells of Cajal = stellate mesenchymal, i.e muscle cells which send long processes into intestinal smooth muscle.

There is a descending gradient in pacemaker frequency.

Function BER coordinates peristalsis & other motor activity

② Spike potentials : i.e True A. potentials that occur at 40 mV

They superimposed on BER & produce increase in muscle tension.

The higher slow wave potential (depol.), the more frequent the spike potentials.

N.B Ca^{++} influx from ECF binds to calmodulin $\rightarrow$ activates MLCK $\rightarrow$ cont.

Enteric nervous system 2 interconnected types :

1 <u>Myenteric (Auerbach's) plexus</u>	2 <u>Submucosal (Meissner's) plexus</u>
--	---

Between outer long. & inner circular ms	Between mucosa & circular muscles
---	-----------------------------------

Motility (mainly)	Secretion (exocrine & endocrine)
-------------------	----------------------------------

N.B Plexuses neurones secrete A.choline, serotonin, GABA & polypeptides

Extrinsic innervation i.e parasymp & symp

1. <u>Parasymp. cholinergic fibres</u> Preganglionic fibres end on cholinergic n. cell plexuses (++) motility & secretion	2. <u>Sympathetic noradrenergic fibres</u> Postganglionic fibres act Directly on smooth ms & glands or via neurones of enteric plexuses (major effect) (--) motility & secretion (cont. of sphincter)
---	---

Movements in gastrointestinal tr. : 2 types discussed page. 19

Gastrointestinal circulation is arranged in a series of parallel circuits

Regulation of G.I.T. : Nervous & Hormonal.

A Nervous Regulation : Short & Long reflexes

- [1] Short reflexes responsible for Self regulation of GIT
- | | |
|------------------|--|
| <u>Stimulus</u> | [<u>Mechanical</u> Stretch of gut wall.
<u>Chemical</u> Food products, change in pH & osmolality.] |
| <u>Receptors</u> | Dendritic endings of neurones of local plexuses. |
| <u>Afferents</u> | Dendrites of " " " |
| <u>Centre</u> | Enteric plexuses. (myenteric & submucosal) |
| <u>Efferent</u> | Axons of neurones of local plexuses |
| <u>Response</u> | [Motility or Secretion
Affect other neurones in plexuses] |

- [2] Long reflexes Centres are brain & sp. cd

a <u>Conditioned reflexes</u>	b <u>Unconditioned reflexes</u>
<u>Acquired</u> <u>Need Training & CC</u> <u>Receptors</u> outside gut visual, auditory & smell Receptor <u>Centre</u> cerebral cortex <u>Example</u> Pavlov's experiment	<u>Inborn</u> <u>Don't need training or CC</u> <u>Receptors</u> in wall of GIT mechano, chemo, or osmoreceptors <u>Centre</u> RF in brain stem <u>Example</u> Vago-vagal reflex

B Hormonal regulation

GI hormones are polypeptides secreted by special mucosal cells APUD cells involved in amino precursor uptake & decarboxylation

According to structure & function, GI hormones are 2 families:

1. Gastrin family : Gastrin hormone & cholecystokinin
2. Secretin family : Secretin, GIP, VIP, glicentin & glucagon (2)

Functions of Saliva

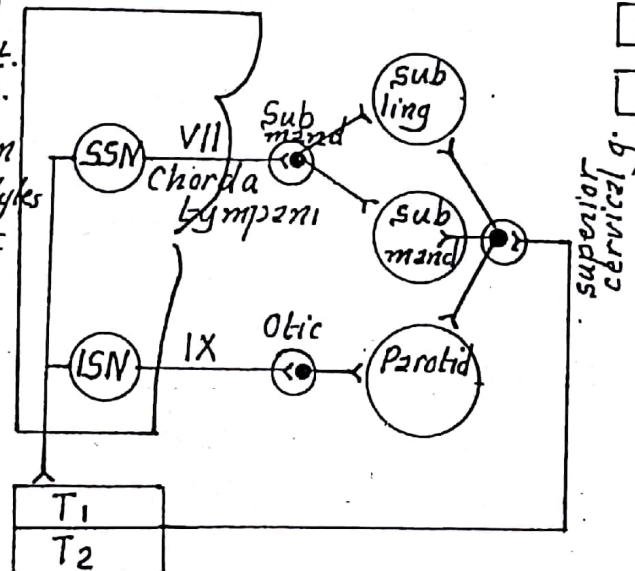
- | | | |
|------------------------------------|------------------------------|------------------------------------|
| a <u>Protection of oral mucosa</u> | b <u>Protection of teeth</u> | c <u>Lubrication & wetting</u> |
| 1 Cooling | 1 Buffers | 1 Articulation |
| 2 Acid buffering | 2 Proline rich pln | 2 Deglutition |
| 3 Ab, lysozymes washing | 3 Flourides | 3 Taste |
| d <u>Digestion</u> | Salivary α amylase | |

Control of salivary secretion

Only NERVOUS

Parasymp

- 1 VD due to VIP
cotransmit. with A.ch.
- 2 Watery secretion
high in electrolytes
low in organic



Sympathetic

- 1 VC
- 2 Viscid secretion
small amount
rich in organic

Conditioned R.

- 1 CC
Sight, Smell, hearing & thinking
stim CC $\rightarrow$ Salivary nuclei
 $\rightarrow$ salivation
- 2 Hypoth Appetat
Taste & smell area in CC
or amygdala $\rightarrow$ stim appetat
 $\rightarrow$ Salivary nuclei
 $\rightarrow$ Salivation

Unconditioned R.

- 1 Taste receptors viz VII IX
 - 2 Thermal & tactile viz V
receptors
 - 3 Stomach & upper
intest. irritation viz X
- 1,2,3 stim. salivary nuclei

N.B Vagal fibres releasing gastrin secrete gastrin releasing peptide i.e not blocked by atropine
Zolinger-Ellison syndrome : Overgrowth of APUD of islets of panc.
 $\rightarrow$ Hyperglycemia $\rightarrow$ ++ HCl $\rightarrow$ duodenal ulcers
Cigarette smoking inhibits secretion of secretin $\rightarrow$ duodenal ulcers
Antibodies against hormones measure conc of hormones by radioimmunoassay & localise secreting cells by immunocytochemical techniques

Mastication chewing Most chewing ms are supplied by 5th cranial n.

Ant. teeth (incisors): cutting force 25 Kg

Post. teeth (molars): grinding force 90 Kg

Chewing reflex is controlled by nuclei in the brain stem

Bolus of food in mouth $\rightarrow$ reflex inhibition of mastication muscles
 $\rightarrow$ drop of lower jaw $\rightarrow$ stretch of mastication ms $\rightarrow$ contraction
 $\rightarrow$ raises lower jaw $\rightarrow$ compresses bolus against mouth $\rightarrow$ of ms

Salivary secretions 2 types of salivary secretory cells

1 Serous cells: secrete serous (watery) secretion containing α amylase.

2 Mucous cells: secrete mucous (viscous) secretion containing mucin

Gland	Parotid	Sublingual	Submandibular	Buccal
% of saliva	25%	5%	70%	
secretory cells	serous	mucous	mixed	mucous

Composition of saliva: 1500 ml / day pH 7

Contents: Mucin, Ptyalin (α amylase) & electrolytes

Hypotonic: Less Na Cl 15 mEq (V_{10} plasma) More K^+ & HCO_3^-

Secretion of saliva: 2 stages

1st stage ACINI secrete Primary secretion, which contains ptyalin & mucin & has the same ionic composition as plasma

2nd stage DUCTS modify primary secretion via aldosterone

$3Na^+$ actively reabsorbed $2K^+$ actively secreted Cl^- follows Na^+
 HCO_3^- " secreted Ducts are relatively impermeable to H_2O (4)

N.B. parasymp. stim ++ Flow of saliva $\rightarrow$ $\ominus$ exchange $\rightarrow$ NaCl & K^+

Functions of saliva

3, 3, 3, 1

a) Protection of oral mucosa

1. Cooling of hot food
2. Acid buffering (oral pH 7) & relieves heartburn if occurs
3. Maintaining healthy oral mucosa by washing bacteria & food remnants, lysozymes, Antibodies Ag A & lactoferrin (bacteriostatic)

b) Protection of teeth & prevention of dental caries viz.

1. Buffers keep oral pH at 7 $\rightarrow$ saturation of saliva with Ca^{++} so teeth don't lose calcium.
2. Fluorides added to drinking H_2O are secreted in saliva and protect teeth enamel.
3. Proline-rich ptns protect teeth enamel & bind toxic tannis.

c) Lubrication and wetting

1. Deglutition mucin acts as lubricant
2. Articulation (speech) needs wet oral cavity
3. Taste buds are stimulated by food dissolved in saliva

d) Digestion: of starch viz salivary α amylase inactivated by HCl in stomach

Control of salivary secretion

Only nervous mechanism

• Innervation of salivary glands: parasymp & symp

1) Sympathetic supply:

Superior & inferior salivary nuclei $\rightarrow$ LHCs of thoracic nerves 1 & 2
 $\rightarrow$ superior cervical ganglion $\rightarrow$ Postgang. fibres to salivary glands
Functions 1 VC 2) Trophic salivary secretion i.e. rich in organic constituents e.g. mucin

2) Parasympathetic supply

Nucleus	Nerve	Ganglion	Glands	Functions
Superior salivary (Medulla)	Facial (VII) (chorda tympani)	Submandib.	Submandib. Sublingual	1 Watery secretion More electrolytes Less inorganic
Inferior saliv. (Medulla)	Glossopharyngeal (IX)	Otic	Parotid	2 VD viz VH

N.B. Atropine (muscarinic blocker) reduces salivary secretion.

● Reflexes that cause salivary secretion conditioned & unconditioned

[1] Conditioned reflexes as shown in Pavlov's experim.

- a Sight, smell, hearing the preparation of food or thinking of food
stim. cerebral cortex $\rightarrow$ stim of salivary nuclei $\rightarrow$ $\uparrow$ salivary secretion
- b Appetite area in hypothalamus is stimulated by taste & smell areas in cerebral cortex or amygdala which in turn stim. salivary nuclei $\rightarrow$ $\uparrow$ saliva

[2] Unconditioned reflexes causes by receptors in GIT Inborn

- a stim. of taste receptors via VII & IX nerves $\rightarrow$ $\uparrow$ saliva
- b stim. of tactile & thermal receptors in mouth via V nerve $\rightarrow$ $\uparrow$ saliva
- b irritant food in stomach & upper s. intestine via X nerve $\rightarrow$ $\uparrow$ saliva

Swallowing Deglutition 3 stages

It is initiated voluntary 1st stage & is completed involuntary
Centre Medulla and lower pons

[a] Buccal (oral) stage

voluntary

Movement of tongue upward & backward $\rightarrow$ bolus of food rolled in pharynx

[b] Pharyngeal stage

involuntary

Bolus of food has to choose one of four ways:

- 1 Nose is closed by elevation of soft palate to close posterior nares
- 2 Mouth is closed by elevation of tongue + contraction of mylohyoid ms
- 3 Larynx is closed by elevation of larynx to be covered by epiglottis
+ contraction of vocal cords + swallowing apnoea
- 4 Successive cont. of superior, middle & inferior pharyngeal sphincters
+ relaxation of pharyngo-esophageal sphincter & upper esophageal v
allowing food to pass to esophagus easily.

Pharyngeal stage is principally a reflex act:

- Stimulus: Food in back of mouth
- Receptors: around openings of pharynx especially on tonsillar pillars
- Centre of swallowing or deglutition: Medulla & lower pons

[C] Esophageal stage

Involuntary

[1] Upper esophageal sphincter: tonically contracted to prevent air entry

[2] Lower esophageal sphincter (Gastroesophageal sphincter): tonically contracted to prevent reflux of HCl $\rightarrow$ Heartburn.

1 & 2 relax only during passage of the bolus (receptive relax)

The tone of LES is under neural control

• Acetylcholine released by some vagal fibres causes LES contraction

• NO & VIP released by interneurons innervated by other vagal fibres causes relaxation of LES (lower esophageal sphincter)

The tone of LES is $\ominus$ in pregnancy by high level of progesterone $\rightarrow$ heartburn

Factors that decrease the pressure in the LES:

1 Certain food: Fat, coffee, chocolate and citrus juices

2 Endocrinal agents: secretin, GIP, VIP, CCK & glucagon.

3 Paracrine agents: PG A & E

4 Neurocrinal agents: Acetylcholine, dopamine & β stimulants

5 ++ cAMP in LES

Factors that increase LES pressure:

1 Gastrin ++ gastric HCl

2 Motilin

High efficiency of LES is due to the fact that LES lies below diaphragm.

so ++ intrabd. p $\rightarrow$ ++ both stomach and LES p.

[3] Travelling along the esophagus - Fluid by gravity

- Food moves along esophageal tube by 2 types of peristalsis:

1 prim. peristalsis: continuation of peristaltic wave in pharynx.

pass from pharynx to stomach in 8-10 sec. Fails to move all food.

2 secondary peristalsis: caused by esophageal distension by remained food.

It continues until food has emptied from esophagus into stomach.

It is caused by esophageal enteric nerve plexuses & partially by vagus

Stomach

- 1 In pylorus & cardiac regions : Gastric glands secrete mucus.
- 2 In body & fundus : Deep glands contain
 - a Parietal (Oxyntic) cells : secrete HCl & intrinsic factor
 - b Chief (zymogen = peptic) cells : " pepsinogen
 - c Neck cells : secrete soluble mucous viz vagal stimulation
 - d Surface epith. cells : insoluble mucous which protects against mechanical friction and HCl.

N.B Many glands open on a common chamber (gastric pit)
Stomach has a very rich blood & lymph supply.
Stomach is supplied by vagus (para) & celiac plexus (sympathetic).

Gastric secretion 2.5 Litre/day pH highly acidic.

Contents Ions H^+ , Cl^- , Na^+ & K^+ , H_2O , Mucus & Intrinsic factor

Enzymes pepsinogen, gelatinase & lipase

N.B At low secretory rate, Na^+ conc. is high & H^+ conc. is low

Acid (HCl) secretion by oxyntic cells viz active process

Concentration of H^+ ions in gastric juice 1 million times its plasma conc.

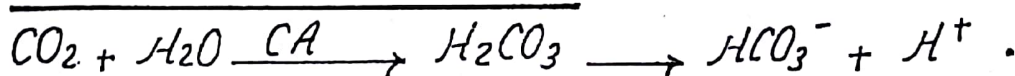
Parietal cells secrete isotonic solution of HCl contains 150 mEq H^+ / litre
conc. of Cl^- 100 mEq & H^+ 0.00004 mEq.

Parietal cells pH, like other cells, is 7 - 7.2

Functions of HCl :

- 1 Maintains sterility of stomach.
- 2 Changes food particles to chyme.
- 3 Activates pepsinogen to pepsin
- 4 Provides optimum pH for pepsin (2)
- 5 Helps iron absorption.
- 6 Helps calcium absorption.
- 7 Stimulates flow of bile.

Mechanism of acid secretion :



Apical mem. : H^+ is pumped in exchange to K^+ (needs ATP & H-K ATPase)

Basal mem. : Cl^- is exchanged for HCO_3^- by Antiport (Cl shift phenomenon)

Cl^- moves down electro-chemical gradient via channels activated by cAMP
 H_2O follows HCl by osmosis.

Alkaline tide for each mol. HCl formed in lumen, a molecule of NaHCO_3 is formed in blood $\rightarrow$ ++ pH of gastric venous blood during HCl secretion.
Stimuli of acid secretion

- 1 Histamine via H_2 receptors $\rightarrow$ ++ intracellular cAMP.
 - 2 Acetylcholine via M_3 receptors $\rightarrow$ ++ intracellular Ca^{++} .
 - 3 Gastrin acts a directly by ++ intracellular Ca^{++} .
b indirectly by ++ histamine from enterochromaffin like cells (EC₁ cells).
- N.B Destruction of oxyntic cells $\rightarrow$ achlorhydria & pernicious anemia.
Ptn Pepsin (cleavage at aromatic acid residues) $\rightarrow$ peptides.

Mechanism of gastric secretion

3 phases

A) Cephalic phase Nervous $\frac{1}{3}$ of gastric secretion via

1 Conditioned reflexes

- a CC : Sight, smell, hearing preparation of food & even thinking of food.
- b Appetite centre of hypothalamus and amygdala.

2 Unconditioned reflexes Food in mouth stimulates taste,

thermal & tactile receptors which send impulses via VII, IX & V cranial nerves

Both 1, 2 stimulate dorsal motor nucleus of vagus

Vagal fibres ++ gastric secretion via release of acetylcholine & GRP.

Proof : Shzm feeding The esophagus is made to open in neck, so that swallowed food doesn't pass to stomach $\rightarrow$ ++ gastric secretion in innervated. Pavlov's pouch & not in denervated Heidenhain pouch of stomach

B) Gastric phase Nervous & hormonal $\frac{2}{3}$ of gastric secretion

- 1 Nervous a. Long vagal-vagal reflex
b. Short local enteric reflex (submucosal plexus)

2 Gastrin hormone Discuss.

C) Intestinal phases Nervous & hormonal mostly inhibitory

a Nervous: enterogastric reflex

b Hormones GIP, secretin, CCK and VIP.

N.B Intestinal gastrin ++ gastric secretion (not important)

Mechanism of inhibition of gastric secretion

A Cephalic phase Depression & fear via impulses from CC inhibit vagal nucleus.

B Gastric phase Drop of pH in pylorus below 3 inhibits gastrin secretion

C Intestinal phase Discuss

Gastric motility

1) Proximal motor unit

- Fundus & stomach body
- Thin wall
- Function Storage of food

2) Distal motor unit

Antrum & pyloric region & sphincter

Thick wall

Mixes food & G. secretion via peristalsis

Partial digestion of food to form chyme

Cont. of antrum followed by pylorus then duodenum i.e. they function as one unit.

Partial cont. of antrum prevents solid masses from entering duodenum & small intestine.
Cont. of pylorus persists longer than duodenum to prevent regurgitation of food.

• Innervation:

1 Vagal parasympathetic inhibitory fibres

i.e. secrete ATP

2 Symp adrenergic inhibitory fibres

3 Enteric nervous system.

Vagal cholinergic excitatory fibres

• Receptive relaxation

Stimulus: Gastric distension

Receptors: Mechanoreceptors

Aff: Vagus & sympathetic

Centre: vagal nucleus & lower 6 thoracic segments

Efferent Vagal parasympathetic & symp adrenergic fibres

Response Stomach relaxation

Basic electrical rhythm BER

Gastric slow waves 3-5 cycles/minute

Some leads to spike burst & in turn peristalsis

At rest, spike burst 3/min

Vagal stim. & Gastrin ++ spikes to 5/min

Peristalsis are stronger & faster in pylorus

NB solid closes pyloric orifice leading to slow gradual gastric emptying (10)

3] Regulation of gastric evacuation (emptying)

1 Gastric factors: G. distension NERVOUS (short & long) $\oplus\oplus$ pyloric pumping
Gastrin

2 Intestinal factors

a Nervous Enterogastric reflex mediated by inhibitory vagal parasympathetic fibres

Presence in duodenum of the followings $\ominus$ pyloric pumping: 6

Increased acidity [Plas [Distension
Irritation [Fats [Hypertonicity

b Hormonal Presence of Fats in the duodenum releases GIP, CCK & secretin collectively called (enterogastrone) which $\ominus$ pyloric pumping.

3 Consistency of food Fluids are evacuated more rapidly than solids

4 Reflexes from outside GIT

a Pain $\ominus$ gastric emptying

b Emotions $\ominus$ or $\oplus\oplus$ gastric emptying

Hunger contraction or Hunger pain

Feeding centre in hypoth. is inhibited by impulses from satiety centre

Hypoglycemia $\ominus$ activity of satiety centre $\rightarrow \oplus\oplus$ activity of feeding

which sends impulses to [Limbic cortex $\rightarrow$ Hunger sensation
[Vagal nucleus $\rightarrow$ Hunger contraction

Vomiting

• Centre: in medulla oblongata & related to respiratory centre.

It is affected by chemoreceptor trigger zone in medulla

• Causes of vomiting:

A) Reflex causes:

mouth 1 Mech. stim. of post. part of tongue

stomach 2 Irritation of gastric mucosa

intest 3 Intestinal obstruction or irritation

4 Visceral pain e.g. renal colic or appendicitis

B) Central causes: stim. CRTZ

1 Drugs e.g. apomorphine & emetine

2 Hypoxia

3 Acidosis

4 Motion sickness: sea & air

Mechanism of vomiting

1 Before vomiting: nausea, salivation, sweating & tachycardia.

2 During vomiting:

Protection of air passages

- a Elevation of soft palate to close nasal cavity
- b Closure of glottis
- c Apnoea

Relaxation of

- a Stomach completely passive
- b LES
- c esophagus

Deep insp. then cont. of

- a Diaphragm
- b Abdominal ms
→ ++ abdom p.s squeeze stom.
- c pyloric sphincter.

Effects of vomiting:

- 1 Dehydration → Hypotension & tachycardia
- 2 Alkalosis due to loss of HCl → Hypoventilation & tetany
- 3 Hypokalaemia

Peptic ulcer

Mucosal barrier is formed of:

- 1 Insoluble mucus
- 2 Integrity of mucosal mem. which:
 - is impermeable to H^+ ions
 - pumps H^+ actively to lumen & Na^+ to interstitial fluid.
- 3 Prostaglandins which
 - ++ mucosal secretion
 - acid secretion
 - ++ Na^+ active transport
 - ++ mucosal blood flow.

Causes of peptic ulcers:

- 1 Break of mucosal barrier by:
 - a Alcohol
 - b Aspirin & nonsteroidal anti-inflammatory
-- PGs (-- mucus & HCO_3^- secretion)
 - c *Helicobacter pylori* bacteria

So, H^+ diffuses from lumen to cell
 Na^+ " from plasma to cell
→ ++ H^+ & Na^+ intracell. conc.
→ destroy of cellular metabolic function
→ ulcer formation.
- 2 Excess HCl secretion
e.g Zollinger-Ellison syndrome.

Treatment of peptic ulcers:

- 1 Inhibition of acid secretion:
 - a Blockage of H_2 receptors e.g by cimetidine
 - b inhibit H^+-K^+ ATPase in apical membrane e.g omeprazole (proton inhibitor)
- 2 Eradication of *Helicobacter pylori* with antibiotics
- 3 Stop use of non-steroidal anti-inflammatory drugs
- 4 Surgical removal of gastrin-secreting tumors.

Pancreatic secretion

Composition 1500 ml/day Alkaline (high HCO_3^- 113 mEq/L).

Panc., intes. & bile juices neutralise HCl, so jejunum contents are neutral & rarely alkaline.

Panc. enzymes are fully sufficient for complete digestion: 3 classes

- 1 Starch Panc amylase (active) maltose, α limit dextrins & maltotriose
- 2 Neutral Fat

Panc lipase (active)	Fatty acids
cholesterol esterase	monoglycerides
phospholipase	glycerol

The action of these enzyme is facilitated by bile salts.

- 3 Proteolytic enzymes inactive
 - a Endopeptidases trypsinogen & chymotrypsinogen
 - b Exopeptidases procarboxypolypeptidase

Enterokinase (in intestine) activates trypsinogen to trypsin.

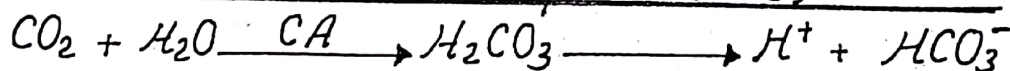
Trypsin, in turn, activates rest of "a", chymotrypsinogen & procarboxypolypeptidase

Trypsin inhibitor is present in pancreas

N.B Ribonuclease (digests RNA) & deoxyribonuclease (digests DNA)

In severe panc. damage or blockage of duct, panc. enzymes are activated in panc.
 → acute pancreatitis (lethal) or life time panc. insufficiency.

Mechanism of secretion of aqueous (HCO_3^-) secretion. In duct cells



- HCO_3^- is actively secreted in lumen by $\text{HCO}_3^-/\text{ATPase}$.

- H^+ is pumped to plasma in exchange with Na^+ ions pumped in duct cells
 Na^+ is passively transport to lumen. H_2O follows Na^+ by osmosis

Acid tide is caused by H^+ ions pumped to bl. It neutralises alkaline tide

Functions of aqueous secretion: 1 It washes out the secreted enzymes
 2 It provides neutral pH for enzymatic activity in intestine.

Regulation of pancreatic secretion Nervous & HORMONAL (more impant)

- 1 Nervous: During gastric & cephalic phases of gastric secretion, vagal fibres increase panc. enzymes from panc. acinar cells via phospholipase C.

2 <u>Hormonal</u>	- Secretin (discuss)	Cholecystokinin (discuss)
	++ aqueous secretion Duct cells via ++ cAMP	++ enzymatic secretion Acinar cells via phospholipase C

Liver and biliary system

Liver lobules (functional unit) consists of hepato-cellular plates radiating from centre vein & empty into hepatic veins. Bile canaliculi lie in between cells

Functions of the liver :

1 Vascular Functions For storage & filtration of blood

- a Liver stores 200-400 ml of blood to replace lost blood in hge
- b Liver macrophages Von Kupffer cells remove 99% of bacteria of portal blood

2 Metabolic Functions:

- a CHO liver plays impor. role in glucostatic mech. refer to endocrine
- b Fat 1 Oxidation of FFA $\rightarrow$ energy 2 Conversion of CHO & ptn to fat
3 Formation of VLDL & LDL 4 Synthesis of 70-80% of ^{cholesterol} phospholip
- c Ptn 1 Deamination of aa before transformation into CHO & fat.
2 Formation of plasma ptn (coagulation F), urea & non essential aa
- d Vitamins Storage of vitamins A, D & B₁₂
- e Storage of iron iron + apoferritin (ptn) $\rightarrow$ Ferritin
- f Detoxification & excretion in bile of drugs (e.g. sulphonamides & penicillin), hormones (thyroxine & steroid hormones) & Ca^{++}

3 Secretory & excretory functions: Formation of bile.

BILE

Composition H₂O 97%, bile salts 0.7%, bile pigments 0.2%, cholesterol 0.06%, inorganic salts 0.7%, Fa 0.15%, lecithin 0.1%, fat 0.1% & alkaline phosphatase

Mechanism of bile secretion

- In between meals: Cont. of sphincter of Oddi $\rightarrow$ secretory p. of liver
So, bile passes to be stored in gall bladder
- During meals 1 Swallowing relaxes sphincter of Oddi
2 Food reaches intestine releases CCK $\rightarrow$ evacuation of G. bladder.
- After meal 95% of bile salts are actively reabsorbed from terminal ileum into portal circ. back to liver i.e. enterohepatic circ. for bile salts. (1

Out of 3.5 g bile salts secreted by liver/day, only 0.2-0.4 g 5% are lost in stool.

Choleretics: Substances which stimulate LIVER to secrete bile
e.g. Acetylcholine, bile salts & secretin (Hydrocholeretic)

Cholagogues: Substances which stim. excretion of G. BLADDER e.g. CCK.

Bile salts Na^+ and K^+ salts of bile conjugated to glycine or taurine (derivative of cysteine). Bile salts are formed from cholesterol

Types of bile acids 1 Primary bile acids 2 Formed in Liver

- cholic acid conjugated with glycine $\rightarrow$ glycocholic acid.
- chenodeoxycholic acid ,, ,, taurine $\rightarrow$ taurocholic acid.

2 Secondary bile salts Formed in colon by bacteria which convert cholic acid to deoxycholic acid & chenodeoxycholic to lithocholic acid

Functions of bile salts:

① Digestion of fats: Bile salts help fat digestion in 2 ways

- Lipids: emulsification - surface tension - Panc lipase: activation.

② Absorption of fatty acids Bile salts are essential for fat absorption via formation of micelles which are bile acid-lipid complexes (water soluble cylindrical discs). Bile salts are amphipathic.

③ Choleretic action: Bile salts are the most powerful choleretics

④ Solvent action: prevent ppt of cholesterol, bilirubin & fatty acids in gall bladder & so prevent formation of gall bladder stones.

N.B Resection of terminal ileum (no bile salt absorption) $\rightarrow$ steatorrhea and severe mal absorption of fat & fat soluble vitamins.

Bile pigments:

Bilirubin is metabolic end product of Hb excreted mostly in stool (brownish)

• RES: old RBCs are destroyed by t. macrophage. The chain of 4 pyrole nuclei of Hb forms biliverdin rapidly reduced $\rightarrow$ bilirubin passes to plasma

• Blood: Bilirubin binds mostly with albumin

i.e. H₂em = unconjugate (Free) = indirect bilirubin

- Liver: Active reuptake by liver cells of bilirubin & not albumin.
4 steps
Binding of bilirubin to cytoplasmic proteins
Conjugation of „ to glucuronic acid in smooth E. reticulum
 → Chole = Conjugate = Direct bilirubin (more H₂O soluble)
Excretion of bilirubin into bile canaliculi by active process

NB Some conjugate bilirubin pass to bl. & bind less tightly to albumin than free bilirubin & excreted in urine

- Intestine: Intestinal mucosa is relatively impermeable to conjugate bilirubin.

- 50% of conjugate bilirubin reduction by bacteria, Urobilinogen (highly soluble)
Fate of urobilinogen

- Most is changed into stercobilinogen & excreted in stool.
 Stercobilinogen oxidized → Stercobilin (brownish color of stool)
- Some is reabsorbed into portal vein & re-excreted by liver back to gut i.e. enterohepatic circulation for bile pigment
- 5% enters systemic cir. & excreted in urine oxidized, urobilin

- Rest of conjugate bilirubin is deconjugated in intestine & absorbed into portal circ & excreted by the liver i.e. enterohepatic circulation.

NB. Plasma bilirubin is of two forms:

<u>Haem = unconjugate = Indirect</u>	<u>Chole = Conjugate = Direct</u>
chief form	Low conc.
Gives indirect Van den Bergh	Gives direct Van den Bergh

Jaundice (icterus)

Def.: Yellowish tint of skin, mucous mem. & sclera caused by hyperbilirubinemia
 (above 2 mg% 70 micromol/L) Normally, bl. bilirubin 0.2-0.8 mg%.

- Causes:
- | | |
|-----------------------------------|-------------------------------------|
| 1 ++ <u>unconjugate bilirubin</u> | 2 ++ <u>conjugate bilirubin</u> |
| a : + production e.g. haemolysis | a -- secretion into bile canaliculi |
| b -- uptake by liver cells | b intrahepatic or extrahepatic |
| c -- binding or conjugation | duct obstruction |

Types: 3 Hemolytic, Obstructive & Hepatic page 17

Type items	Hemolytic prehepatic	Obstructive posthepatic cholestatic	Hepatic hepatocellular
Cause	Hemolytic anemia	Obstr. of bile ducts stone, cancer head of pancreas	Damage of liver cells itis, chemicals or drugs
Mech.	+++ Form. of hem. bilirubin ++ uptake by liver ++ excretion of stercobilin urobilin	Regurgitation to bl. excretion in urine of cholebilirubin	Liver is unable to: take all hembilirubin excrete all cholebilirubin
Characters			
• blood	++ Hem bilirubin	++ Chole bilirubin ++ bile salts	++ Chole & hem bilirubin ++ bile salts
Van den Berg	Indirect	Direct	Biphasic
• urine	++ urobilin. pale	+++ cholebilirubin very dark +++ bile salts	++ cholebilirubin dark ++ bile salts
• Stool	++ stercobilin very dark	--- stercobilin very pale Steatorrhea	-- stercobilin pale Steatorrhea (greasy)
• Liver function tests	normal	++ cholesterol alkaline phosphatase	Impaired

N.B. bile salts in blood → pruritis (itching) & bradycardia.

Functions of gall bladder

1. Storage of bile secreted by liver in between meals
2. Concentration of bile Gall bladder capacity 20-60 ml, yet it stores 450 ml (12 H secretion) viz concentration of bile by H_2O absorption
Mechanism Active Na transport is followed by passive absorpt. of Cl^- , HCO_3^- & H_2O
3. Prevention of marked rise of intrabiliary pressure. viz concentration of bile
4. Acidification of bile to prevent ppt of constituent of concentrated bile as lecithin, bile salts & cholesterol
Mechanism Absorption of HCO_3^- ; so gall bladder bile contains 10 mEq/L HCO_3^- while liver bile contains 28 mEq/L.
5. Secretion of white bile (mucous) to protect gall bladder & bile duct mucosa from the concentrated acidified bile.
6. Emptying of the gall bladder During food intake viz

a cholecystokinin (CCK): released in response to fatty acids & amino acids

b vagal stimulation: less strong than CCK.

Vagal stim. occurs directly during cephalic stage and indirectly via vagovagal reflex during gastric stage

Effects of cholecystectomy: bile empties continuously & slowly in intestine allowing fat digestion & good health. Only avoid high fat meals.

Small intestine

280 cm in a living human, 40% jejunum & 60% ileum

Digestion is completed in the lumen or in intestinal mucosal cells

Absorptive surface is increased 800 times to 200 m^2 by valvulae conniventes, villi $20-40/\text{mm}^2$ & microvilli (brush border) $\rightarrow$ out of 9 L/day of intestinal fluid only 2 L/day pass into colon.

Paneth (endocrine) cells in depth of crypts secrete defensins (antibiotics)

Secretion of small intestine

<u>1 Mucus Functions</u>	<u>Secreted by</u>	<u>Stimulated by</u>
1 Covers, protects & lubricates	1 Surface epith.	1 Ch & physical irritation
2 binds to some bacteria	2 Goblet cell	2 Cholinergic fibres
3 " to immunoglobulins	3 Brunner's gl. s. intestine duodenum	3 Hormones e.g. secretin

2 Enzymes At brush border (not secreted)

peptidases, disaccharidases & lipase.

Life span of intes. cell is 2-5 days i.e. 17 billion cell (30 g ptm) are shed/day.

3 Intestinal alkaline fluid 1800 ml/day pH 7.5-8
Formed by crypt cells Isotonic fluid of NaCl & NaHCO_3^-

Regulation of s. intestinal secretion

- 1 Local nervous reflexes most important
Initiated by physical (distension) or chemical (chyme) stimuli
- 2 Hormonal regulation
 - a Secretin & CCK $\oplus\oplus$ intestinal secretion
 - b VIP $\oplus\oplus$ electrolytes & H_2O . So, VIP tumour severe diarrhea (18)

Movement of small intestine

2 types

1 Propulsive movements : e.g peristalsis

- Description : Stimulus : stretch of one point of gut
Response : circular cont. behind & relax. in front of the bolus

They propagate oral to caudal direction at a rate of 2-25 cm/sec.

They move the chyme at a rate of 1 cm min i.e 3-5 hours are required for chyme to pass from pylorus to ileocecal valve

- Control : Enteric n.s which is regulated by autonomic n.s
Stretch cause neurones to release Calcitonin Gene Related Polypeptide & serotonin
Contraction behind is produced by acetylcholine & substance P
Relaxation in front is produced by VIP, NO or ATP

- Function : Propagation of food

N.B Peristalsis rush Cause : irritation of intestinal mucosa

It is powerful & rapid; within minutes it sweeps intes. content into colon.

Control Centre brain stem. Extrinsic n. reflex & Direct ++ myenteric plexus reflex

Peristalsis is blocked if a segment is removed & reversed before it is sewed on

Gastroenteric (gastro ileal) reflex Stimulus : Gastric distension

Response ++ peristalsis in small intestine

Mediated by myenteric plexus

Intestinal motility $\oplus$ by gastrin, CCK, serotonin & insulin
 $\ominus$ by secretin, & glucagon

Ileocecal valve & ileocecal sphincter (thickened muscle at end of ileum)

• Relaxation is due to : Gastro-ileal reflex and Gastrin hormone

• Contraction is due to : Distension or irritation of cecum.

via myenteric reflex & extrinsic sympathetic reflex

2 Segmentation (mixing) movements : Most frequent

- Description : In a long loop of intestine, several constrictions divide the loop into equal segments (few cms). After few seconds, new appear

in the middle of each segment solid constrictions disappear & so on.

- Control: Myogenic controlled by BER (slow waves). However, contractions become effective only by enteric n.s. i.e. become weak by atropinisation.
- Function: 1 Digestion: they mix chyme with digestive juices
2 Absorption: Allows contact of food with mucosa.

Large intestine

Innervation of colon:

- 1 Sympathetic n.s.: inhibitory via lesser splanchnic nerve
- 2 Parasympathetic n.s.: excitatory via vagus (proximal $\frac{1}{2}$ of colon)
Pelvic nerve (distal $\frac{1}{2}$ of colon).

N.B. Ext. anal sphincter (skeletal voluntary) via 1 & 2 Sacral & pudendal nerve

Colon, 100 cm in living adult, has 3 teniae coli i.e. bands of longitudinal ms shorter than colon $\rightarrow$ outpouchings (haustra). It has no villi.

Colonic glands secrete: mucus. Colon motility:

Ileocecal valve projects slightly into cecum. It is normally closed & opens briefly by peristalsis to permit some ileal chyme into colon.

Gastro-ileal reflex increases passage of chyme through ileocecal valve.

Colon motility is coordinated by slow waves $\oplus$ from 2/min at " " to 8/minute at sigmoid.

Types of movements: 2 types

A) Mixing movements

1 Segmentations: similar to small intestine

2 Haustriation modified segment.

allows absorption of fluid & dissolved substance

B) Propulsive movements

1 Peristalsis: rare

2 Mass movement: modified peristalsis

Mass movements occur few times each day. Often after breakfast.

• Description: simultaneous cont. over a large area of colon.

• Control: due to gastro-colic & duodeno-colic reflexes mainly via

extrinsic autonomic nerves. Gastrin also stim. gastro-colic reflex.

- Function: Moves fecal material en masse from colon to rectum $\rightarrow$ disten.

Absorption in colon Great capacity i.e. 90% of 2L reaching colon. Na^+ is actively absorbed, Cl^- & H_2O follow passively. K^+ & HCO_3^- are secreted.

Clinical application: Rectal drug administration especially in children. Na^+ absorption & K^+ secretion are controlled by aldosterone.

Defecation

Preparatory reflexes: Mass movements (discuss)

Spinal parasympathetic reflex:

- Stimulus Rectal distension.
- Receptors Mechanoreceptors.
- Afferent Pelvic nerve.
- Centre 2, 3 & 4 sacral segments.
- Efferent Pelvic nerve.
- Response Contraction of rectal wall & relax of internal anal sphincter.

This reflex occurs in newly born & in persons with TS of sp. rd above sacral 2,3

Voluntary control of defecation:

- A) Conditions are acceptable B) Conditions are not acceptable

Excitatory impulses CC sends to sacral centre Inhibitory impulses

Relaxes External anal sphincter Contracts

Deep breath + Abdom. ms cont.

N.B Dietary Fibres e.g. cellulose and lignin act as bulk laxative (not digested)

Transit time in colon 1st part of a test meal reaches

- cecum in 3-4 hours
- hepatic flexure 6 hours
- splenic flexure 9 hours
- pelvic colon 12 hours

Intestinal bacteriz: Form vitamin K & B complex

Form gases in flatus Great mass of bacteriz pass in stool. (21)

Gastro-intestinal absorption

At tip of villous there is capillary tuft drains in portal vein
lacteal lymphatic v into thoracic duct

Absorption of H_2O & Electrolytes:

Small amount of H_2O is absorbed in colon or via gastric mucosa
25-35 g Na^+ i.e. $\frac{1}{2}$ body content of Na^+ are absorbed in S. intestine

Mechanism of Na^+ absorption: similar to that in kidney

At basolateral border: Na^+ is actively absorbed by Na^+-K^+ ATPase

Results: Cl^- follows passively

H_2O follows by osmosis 8.5 L in small & 0.3 L in large intestine

K^+ or H^+ is secreted in exchange for Na^+

Meal enters jejunum has the same osmolality of plasma

At luminal border Na^+ is passively absorbed from 142 to 50 mEq/L

Results Cotransport of glucose, galactose or amino acid

i.e. absorption of Na^+ is import. for glucose absorption & vice versa

Mechanism of K^+ absorption & secretion

In proximal part of colon, K^+ is absorbed along electro-chemical gradient

In distal part of colon, K^+ is secreted in exchange with Na^+ via aldosterone
i.e. secondary active secretion.

Mechanism of Ca^{++} absorption: mainly in Duodenum.

- At luminal border: by facilitated diffusion.

- At basolateral border: by an active process.

It needs Ca^{++} ATPase active transport system.

It $\uparrow$ by $1,25(OH)_2CC \rightarrow \uparrow \uparrow mRNA \rightarrow \uparrow \uparrow$ Calbindin

Mechanism of iron absorption mainly in Duodenum

- In gastric lumen: Vit C reduces Fe^{++} to Fe^{+} & HCl dissolves Fe^{++}

- In enterocytes: Carrier ptns are needed at both borders

- In blood: Iron is carried on B. globulin (transferrin)

Absorption of H_2O soluble vitamins:

- Vitamin B₁₂

Stomach : B_{12} binds to intrinsic factor

Lower ileum : B_{12} intrinsic factor complex is absorbed by pinocytosis by aid of pancreatic trypsin

Liver : Storage

Vitamin C & rest of B vitamins Absorbed in upper small intestine by facilitated transport or Na dependent active transport

Absorption of Fat soluble vitamins in upper small intes. as part of micelles

CHO digestion and absorption

All disaccharides (sucrose & lactose) & polysaccharides (starches) must be digested by saliv. & panc. α amylases and intestinal disaccharidases to monosaccharides (glucose, galactose & fructose)

Glucose & galactose absorption Na dependent transport.

- At luminal border Cotransport with Na i.e. Secondary active transport
- At basolat. border Facilitated diffusion

Mechanism of Fructose absorption : Na independent transport.

Facilitated diffusion using different carrier.

N.B Pentoses are absorbed by simple diffusion

Ptn & nucleic acids

Absorbed ptns come from 2 sources:

- 1 Endogenous 50% : digestive juices 25% desquamated cells 25%
- 2 Exogenous 50% : i.e. ingested ptns in food

Ptn digestion :

- 1 In stomach Ptn Pepsin $\rightarrow$ polypeptides which act as secretagogues stim. secretion of pancreatic proteolytic enzymes.
- 2 In small intestine in 3 sites lumen, brush border & cytoplasm. Polypeptides Pancr & intes. proteolytic eng. small peptides & aa

Ptn absorption : 4

- 1 aa : At least 7 different carriers transport aa into enterocytes

5 of these carriers are Na⁺ dependent (carry Na & aa)
In enterocytes absorbed aa & aa released from peptides inside cells are transported along basolat. border by at least 5 transport systems to enter portal blood.

[2] Di and tripeptides are transported into enterocytes by a system that requires H⁺ instead of Na⁺

[3] Significant amounts of small peptides also enter portal blood

[4] Very little large peptides or ptns enter portal blood e.g. Fish, egg white and legumes which may lead to allergy.
or Ig A in maternal colostrum → passive immunity to infant

Nucleic acids

Nucleic acids panc nucleases → nucleotides mucosal enzymes → nucleoside
+ phosphoric acid. Nucleosides split → sugar purine & pyrimidine bases
These bases are absorbed by active transport.

Lipid digestion Mostly in duodenum by pancreatic lipases

- Fats are 1st emulsified by bile salts, lecithins & monoglycerides

- Panc. lipases are activated by: (one of 2 mechanisms)

[a] Colipase attached to lipase and activated by trypsin in intestine

[b] Bile salts (salt activated lipase) which hydrolyses cholesterol esters, esters of fat sol. vitamins, phospholipids and triglycerides
Triglycerides panc. lipase → FFA + 2 monoglycerides
cholesterol esters cholesterol esterase → fatty acids + free cholesterol
Phospholipid phospholipase A₂ → fatty acids

N.B 30% of dietary triglycerides digested by lingual lipase activated in stomach
Gastric lipase is only important in pancreatic insufficiency

Fat absorption 3

[1] Micelle formation in intestinal lumen i.e. cylindrical aggregates (24)

- centre of emulsified products of fat digestion & fat soluble vit.
- shell of bile salts which solubilises lipid i.e. H₂O soluble.

At brush border Contents are released & absorbed by simple diff. and bile salts are decomposed to form new micelles.

When all lipids are absorbed, bile salts are actively absorbed in the ileum back to liver by enterohepatic circulation.

2 Chylomicron formation in intestinal cells

Absorbed fatty acids + 2 monoglycerides $\rightarrow$ triglycerides

In smooth endoplasmic R.: triglycerides, cholesterol & phospholipid form chylomicrons i.e. small lipid droplets covered by β lipoproteins (from intest. cells)

At basolateral borders Chylomicrons are absorbed by exocytosis.

3 Transport of lipids into circulation

(a) 80-90% of fats: Chylomicrons fuse into larger droplets which are absorbed via lymphatics i.e. central lacteals of villi

(b) Short chain fatty acids (more H_2O soluble): absorbed into portal blood

N.B Cholesterol is incorporated into chylomicrons & absorbed in lymphatic
Non absorbable plant sterol in soybeans reduce cholesterol absorption by competing with cholesterol for esterification with fatty acids

Paralytic ileus = adynamic ileus

Cause trauma to s. intest. or peritoneal irritation during abdom. operation

$\rightarrow$ ++ noradrenergic discharge in splanchnic n. $\rightarrow$ -- intest motility

$\rightarrow$ -- intest. absorption $\rightarrow$ ++ fluid in intest. $\rightarrow$ more stretch in intestine +ve feedback $\rightarrow$ -- intest motility (starting at ileum)

!!! Aspiration of fluid by intestinal tube until peristalsis recurs

Abnormality in swallowing

1 Dysphagia Difficulty in swallowing

Cause pharyngitis, poliomyelitis or myasthenia gravis

2 Achalasia Failure of LES to relax following swallowing

Cause Absence of internal nervous plexus in esoph. smooth m.
Result accumulation of food & dilatation of lower esophagus

Constipation

Symptoms Abdom. discomfort, headache, nausea & loss of appetite

Causes 1 Repeated inhibition of desire of defecation (most common)

2 -- muscular activity of L. intestine due to: emotional stress,

weakness & lack of exercise & diet poor in cellulose i.e. fruits & vegetables

ttt 1 Advise not to inhibit the desire for defecation

2 Improve muscular activity of L. intestine ≠ causes

3 Symptomatic ttt a laxatives i.e. lubricants e.g. liquid paraffin

b Purgatives unabsorbed solutes ($MgSO_4$) → -- H_2O reabsorpt.

c Enema. e.g. glycerin enema

Diarrhea Cause irritation of small intestine e.g. bact or virus infect.

Results Dehydration, loss of Na^+ & K^+ metabolic acidosis (-- HCO_3^-)

Megacolon (Hirschsprung's disease)

Cause Congenital absence of myenteric & submyenteric plexuses in a segment of distal colon → spasm of this segment

→ distension of L. intestine above → defecation every few months

ttt Resection of the affected segment

CHO malabsorption

1 Deficiency of one or more of the disaccharidases

Result 1 Diarrhea: unabsorbed oligosaccharides draw H_2O by osmosis

2 Flatulence unabsorbed oligosacchar bacteria → $CO_2 + H_2$

2 Lactose intolerance Most common cause of CHO malabsorp.

Cause -- lactase enzyme → intolerance to milk.

ttt Commercial lactase preparation

Intake of yoghurt (not milk) which contains bact. lactase.

Lipid malabsorption more common than CHO or ptn malabsorp

1 Diseases of exocrine portion of pancreas (-- lipase & -- HCO_3^-) 26
i.e. relatively acidic medium → inhibits panc. lipase & ppt some bile salts

Result impaired digestion & absorption of fat $\rightarrow$ steatorrhea

2 Defective absorption of bile salts in distal ileum.

Cause Resection or Tropical sprue or coeliac disease of distal ileum

3 Liver diseases $\rightarrow$ -- secretion of bile.

Ptn malabsorption Due to congenital defect in mechanism that transports neutral aa (Harnup disease) or basic aa (Cystinuria).

NB ptn is stool (not dietary) but comes from bact & cellular debris

GOOD LUCK
